

Serial No. 10/630,633

6102-000068/US

Amendment A and response to Office Action dated October 5, 2007

April 3, 2008

IN THE SPECIFICATION

Amendment of the specification is requested under 37 C.F.R. §1.121(b)(3). Please replace the existing specification. As required by 37 C.F.R. §1.121(b)(3)(ii), a substitute specification is attached hereto in both “mark-up” and “clean” form in compliance with 37 C.F.R. §1.125(c). Applicant states in accordance with 37 C.F.R. §1.125(b) that the substitute specification includes no new matter.

## IN THE CLAIMS

The following listing of claims will replace all prior versions and listings of claims in the present application.

1. (Currently amended) **Transdermal A transdermal** therapeutic system (TTS) comprising an active-substance-containing cement matrix, ~~characterized in that~~ wherein the cement matrix ~~contains~~ comprises a hot-melttable adhesive in which the active substance, ~~Rotigotine ((-)-5,6,7,8-tetrahydro-[propyl[2-(2-thienyl)ethyl]-amino]-1-naphthol)~~, is dispersed and partly or completely dissolved, and wherein the active substance is rotigotine.
2. (Currently amended) The TTS ~~[[as in]]~~ of claim 1, ~~for which~~ wherein the active-substance-containing cement matrix is produced by preparing a solvent-free melt of the cement matrix and metering the ~~Rotigotine~~ rotigotine into the solvent-free melt ~~of the cement matrix~~ at a temperature ~~[[of]]~~ between 70°C~~[[.]]~~ and 200°C.
3. (Currently amended) The TTS ~~[[as in]]~~ of claim 1, ~~or 2, in which~~ wherein the hot-melttable adhesive ~~consists of a mixture of~~ comprises an amine-resistant silicone adhesive and, in mixture therewith, at least one suitable pharmaceutically acceptable softener.
4. (Currently amended) The TTS ~~[[as in]]~~ of claim 3, ~~in which~~ wherein the at least one softener is an organic wax.
5. (Currently amended) The TTS ~~[[as in]]~~ of claim 3, ~~or 4, in which~~ wherein the at least one softener is ceresine or ozokerite.
6. (Currently amended) The TTS ~~as in one of the preceding claims, in which the percentile proportion of the Rotigotine in~~ of claim 1, wherein the cement layer is matrix comprises 4-40 weight % rotigotine.
7. (Currently amended) The TTS ~~as in one of the preceding claims, in which the percentile proportion of the Rotigotine in~~ of claim 1, wherein the cement layer is matrix comprises 9-30 weight % rotigotine.

8. (Currently amended) ~~The TTS as in one of the claims 1-6, in which the percentile proportion of the Rotigotine in of claim 1, wherein~~ the cement layer is matrix comprises 20-40 weight % rotigotine.
9. (Currently amended) ~~The TTS as in one of the preceding claims, in which of claim 1, wherein~~ the ~~Rotigotine~~ rotigotine is present ~~as the biocatalytic in free-base form~~.
10. (Currently amended) ~~The TTS as in one of the preceding claims, in which of claim 1, wherein~~ the active-substance-containing cement matrix ~~additionally contains further comprises~~ an internal-phase component selected from the group consisting of
- (a) hydrophilic ~~[[or]]~~ and amphiphilic polymers and mixtures thereof with pharmaceutically acceptable softeners,
  - (b) hydrophilic ~~[[or]]~~ and amphiphilic copolymers and mixtures thereof with pharmaceutically acceptable softeners,
  - ~~(c) mixtures of (a) and/or (b) with pharmaceutically acceptable softeners~~
  - ~~[[d)] (c)~~ condensates ~~[[from]] of~~ glycerin and fatty acids, ~~[[or]]~~
  - (d) condensates of glycerin and polyols, and
  - (e) suitable mixtures of ~~[[the]]~~ components (a)-(d).
11. (Currently amended) ~~The TTS [[as in]] of claim [[10]] 1, in which wherein~~ the active-substance-containing cement matrix further comprises at least one internal-phase component ~~[[is]]~~ selected from the group consisting of polysaccharides, substituted polysaccharides, polyethylene oxides, polyvinyl acetates, polyvinyl pyrrolidones, copolymers ~~[[from]] of~~ polyvinyl pyrrolidone and ~~(poly)vinyl polyvinyl~~ acetate, polyethylene glycol, polypropylene glycol, copolymers ~~[[from]] of~~ ethylene and vinyl acetate, glycerin-fatty acid esters as well as and mixtures of polyvinyl alcohol with glycerin.
12. (Currently amended) ~~The TTS [[as in]] of claim 1, characterized in that wherein~~ the cement matrix comprises
- (a) 50-99 weight % of a hot-melttable adhesive,
  - (b) 4-40 weight % ~~Rotigotine~~ of rotigotine,
  - (c) 0-40 weight % of an internal-phase component, and

- (d) 0–10 weight % of other adjuvants.
13. (Currently amended) The TTS ~~[[as in]]~~ of claim 12, ~~for which~~ wherein the hot-melttable adhesive ~~(a)-selected~~ is ~~[[a1]]~~ an EVA adhesive, ~~[[a2]]~~ an SXS adhesive, or ~~[[a3]]~~ a mixture of (i) 70–99 weight % of an amine-resistant silicone adhesive and (ii) 1–30 weight % of a suitable pharmaceutically acceptable softener.
14. (Currently amended) The TTS of claim 1, ~~for the continuous transdermal administration of Rotigotine, characterized in that, wherein, upon application of the TTS on skin of a human patient, an average plasma concentration of 0.4 to 2 ng/ml rotigotine is induced in the patient~~ for a period of at least 5 days following ~~[[its]]~~ said application ~~on human skin, said TTS induces in the patient an average plasma concentration of 0.4 to 2 ng per ml Rotigotine.~~
15. (Currently amended) The TTS ~~[[as in]]~~ of claim 14, ~~characterized in that the TTS induces in the patient wherein~~ an average plasma concentration of 0.4 to 2 ng/ml Rotigotine rotigotine is induced in the patient for a period of at least 7 days following said application.
16. (Currently amended) The TTS ~~as in one of the preceding claims of claim 1, characterized in that the Rotigotine wherein, upon application of the TTS on skin of a human patient, rotigotine~~ is transported through the skin at a steady-state flux rate of 200–300 µg per hour.
17. (Canceled)
18. (Currently amended) Method A method for ~~producing~~ preparing a TTS that ~~encompasses~~ comprises a rotigotine-containing cement matrix, ~~containing Rotigotine as the active substance, characterized in that prior to their lamination the method comprising melting and homogenizing~~ components of the cement matrix ~~are melted and homogenized, solvent-free, in an extruder at temperatures a temperature~~ between 70°C~~[[.]]~~ and 200°C prior to lamination of the components.
19. (Canceled)

20. (Currently amended) ~~Use of Rotigotine in the production of~~ A method for preparing a TTS ~~that comprises a rotigotine-containing cement matrix by the hot-melt method, characterized in that the Rotigotine is introduced, the method comprising pre-melting and homogenizing components of the cement matrix other than the rotigotine, solvent-free, the Rotigotine is introduced and introducing rotigotine at temperatures~~ a temperature between 70°C[[.]] and 200°C[[.]], ~~[[in]] into the [[TTS]] pre-melted cement matrix that has been premelted without solvents.~~
21. (Currently amended) ~~Method or use as in one of the preceding claims, whereby~~ The method of Claim 20, wherein the ~~hot-melting process takes place~~ rotigotine is introduced into the pre-melted cement matrix at temperatures a temperature between 120°C[[.]] and 160°C.
22. (Currently amended) ~~Method or use as in one of the preceding claims, whereby~~ The method of Claim 20, wherein the ~~Rotigotine~~ rotigotine is introduced[[,.]] in solid state into the pre-melted cement[[-.]] matrix ~~melt, in its solid state.~~
23. (Currently amended) ~~Method or use as in one of the preceding claims, whereby~~ The method of Claim 20, wherein the rotigotine in the cement matrix, ~~produced by the hot-melting process, contains Rotigotine at~~ so prepared has a purity level of at least 98% as measured by HPLC at 220 nm and 272 nm.
24. (New) The method of Claim 18, wherein the melting takes place at a temperature between 120°C and 160°C.
25. (New) The method of Claim 20, wherein the rotigotine in the cement matrix so prepared has a purity level of at least 98% as measured by HPLC at 220 nm and 272 nm.